

**WHAT IS CLAIMED IS:**

- 1) An aqueous dispersion of hydrogel nanoparticles, comprising:  
interpenetrating polymer network ("IPN") nanoparticles, wherein each IPN nanoparticle comprises a first polymer interpenetrating a second polymer; and  
an aqueous medium;  
wherein, the IPN nanoparticles are substantially free of a shell and core polymer configuration; and the aqueous dispersion of hydrogel nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon.
- 2) The aqueous dispersion of hydrogel nanoparticles of claim 1, further comprising a biologically active material.
- 3) The aqueous dispersion of hydrogel nanoparticles of claim 2 wherein the biologically active material is: a drug, a pro-drug, a protein, or a nucleic acid.
- 4) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the stimulus comprises a change in temperature.
- 5) The aqueous dispersion of hydrogel nanoparticles of claim 4, wherein the temperature change above a gelation temperature ("T<sub>g</sub>") induces a volume phase transition of the IPN nanoparticles, resulting in an inverse thermo-thickening property of the aqueous dispersion of hydrogel nanoparticles.
- 6) The aqueous dispersion of hydrogel nanoparticles of claim 5, wherein the inverse thermo-thickening property is a transformation from a low-viscous fluid to a gel when heated above the T<sub>g</sub>.
- 7) The aqueous dispersion of hydrogel nanoparticles of claim 5, wherein the T<sub>g</sub> is about 34°C.

- 8) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer comprises poly(N-isopropylacrylamide) or hydroxypropylcellulose.
- 9) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the second polymer comprises poly(acrylic acid).
- 10) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer comprises poly(N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid).
- 11) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the mono-disperse nanoparticles have a uniform sized hydrodynamic radius.
- 12) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the mono-disperse nanoparticles have an average hydrodynamic radius in the range from about 75 nm to about 200 nm.
- 13) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer and second polymer in the mono-disperse nanoparticles have weight ratio of about 1:1.88.
- 14) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer and the second polymer form a total polymer having a concentration range from about 1.25 wt% to about 5.25 wt% in distilled water.
- 15) A method of preparing an interpenetrating polymer network ("IPN") of mono-disperse nanoparticles, comprising:
  - (a) providing a first mono-dispersed polymer nanoparticle prepared by mixing a first monomer, a surfactant, a first cross linking agent, and a first initiator at a first temperature;
  - (b) adding to the first mono-dispersed polymer nanoparticle a second monomer, a second cross linking agent, a second initiator and an activator forming a nanoparticle solution;

- (c) mixing the nanoparticle solution for a period of time at a second temperature to form the IPN of mono-disperse nanoparticles; and
- (d) isolating the IPN of mono-dispersed nanoparticles;
- wherein the first monomer, the first cross linking agent, the second monomer, and the second cross linking agent are substantially free from dissolved oxygen gas.
- 16) The method of claim 15, further comprising (e) mixing the isolated IPN of mono-dispersed nanoparticles with a biologically active material at a third temperature.
- 17) The method of claim 16, wherein the biologically active material is a drug, a pro-drug, a protein, or a nucleic acid.
- 18) The method of claim 16, wherein the third temperature is below a gelation temperature ("T<sub>g</sub>") of the IPN of mono-disperse nanoparticles in an aqueous mixture.
- 19) The method of claim 18, wherein the T<sub>g</sub> is about 33°C.
- 20) The method of claim 15, wherein the first mono-disperse polymer comprises poly(N-isopropylacrylamide) or hydroxypropylcellulose.
- 21) The method of claim 15, wherein the second monomer comprises poly(acrylic acid).
- 22) The method of claim 15, wherein the first mono-dispersed polymer nanoparticle comprises poly(N-isopropylacrylamide) and the second monomer comprises acrylic acid.

23) The method of claim 15, wherein the first cross linking agent comprises N,N'-methylenebisacrylamide; the second cross linking agent comprises N,N'-methylenebisacrylamide; the first initiator comprises potassium persulfate; the second initiator comprises ammonium persulfate; the surfactant comprises sodium dodecyl sulfate ("SDS") and the activator comprises TEMED.

24) The method of claim 15, wherein the IPN of mono-dispersed nanoparticles have an average hydrodynamic radius in the range from about 75 nm to about 200 nm.

25) The method of claim 15, wherein the period of time is less than 130 minutes.

26) The method of claim 25, wherein the period of time about 120 minutes.

27) The method of claim 15, wherein the first temperature is about 70°C.

28) The method of claim 15, wherein the second temperature is about 21°C.

29) A method of preparing a nanocluster of cross-linked interpenetrating polymer networks ("IPN") nanoparticles, comprising:

- (a) providing a dispersion of IPN nanoparticles;
- (b) adding a first cross linking agent and a second cross linking agent to the dispersion of IPN nanoparticles, forming an IPN cross linking solution; and
- (c) heating the IPN cross linking solution to a first temperature for a period of time forming the nanocluster of cross-linked IPN nanoparticles;

wherein, the mono-dispersed IPN nanoparticles have a uniformed size and comprise a first polymer interpenetrating a second polymer and is substantially free from a shell and core polymer configuration; the mono-dispersed IPN nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon.

- 30) The method of claim 29, further comprising (d) mixing the nanocluster of cross-linked IPN's with a biologically active material at a second temperature.
- 31) The method of claim 30, wherein the biologically active material is a drug, a pro-drug, a protein, or a nucleic acid.
- 32) The method of claim 30, wherein the second temperature is below a gelation temperature ("T<sub>g</sub>") of the nanocluster of cross-linked IPN nanoparticles in an aqueous dispersion.
- 33) The method of claim 32, wherein the T<sub>g</sub> is about 33°C.
- 34) The method of claim 29, wherein the first polymer comprises poly(N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid).
- 35) The method of claim 29, wherein the first cross linking agent comprises 1-ethyl-3(3-dimethylaminopropyl) carbodiimide hydrochloride ("EDAC"); and the second cross linking agent comprises adipic acid dihydrazide.
- 36) The method of claim 29, wherein the nanocluster of cross-linked IPN's an average hydrodynamic radius in the range from about 155 nm to about 250 nm.
- 37) The method of claim 36, wherein the nanocluster of cross-linked IPN's have an average hydrodynamic radius in the range from about 225 nm to about 240 nm.
- 38) The method of claim 29, wherein the period of time is about 25 to about 45 minutes.
- 39) The method of claim 38, wherein the period of time is about 33 to about 37 minutes.
- 40) The method of claim 29, wherein the first temperature is about 44°C.

- 41) A nanocluster of cross-linked interpenetrating polymer network ("IPN") nanoparticles, comprising: at least two IPN nanoparticles linked by a cross-linking group; wherein, the each IPN nanoparticle have a uniformed size and comprise a first polymer interpenetrating a second polymer and is substantially free from a shell and core polymer configuration.
- 42) The nanocluster of claim 41, further comprising a biologically active material.
- 43) The nanocluster of claim 42, wherein the biologically active material is a drug, a pro-drug, a protein, or a nucleic acid.
- 44) The nanocluster of claim 41, wherein the first polymer comprises poly(N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid).
- 45) The nanocluster of claim 41, wherein the cross linking group comprises adipic acid dihydrazide.
- 46) The nanocluster of claim 41, wherein the uniformed sized nanoparticles have an average hydrodynamic radius in the range from about 155 nm to about 250 nm.
- 47) The nanocluster of claim 46, wherein the nanoparticles have an average hydrodynamic radius in the range from about 180 nm to about 1000 nm.